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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,121	04/07/2006	Elena Feinstein	71212-A-PCT-US/JPW/JW	1972

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
08/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,121	FEINSTEIN ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-45* is/are pending in the application.

4a) Of the above claim(s) *30-36 and 40-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/28/09, 08/10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and SEQ ID No. 1 in the reply filed on 05/15/2009 is acknowledged. The traversal is on the ground(s) that there would not be a serious burden on the examiner if restriction were not required because a search of the prior art would identify art for any of the other groups. This is not found persuasive because as stated in the previous Office action, the groups as recited do not relate to a single general inventive concept because they lack the same or corresponding technical feature or is found in the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Application

Claims 26-45 are pending. Claims 26-29 and 37-39 are currently under examination. Claims 30-36 and 40-45 and non-elected subject matter are withdrawn as being drawn to a non-elected invention.

Information Disclosure Statement

The submission of the Information Disclosure Statements on 08/10/2007 and 05/28/2009 is in compliance with 37 CFR 19.7. The information disclosure statements have been considered by the examiner and signed copies have been placed in the file.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26-29 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao et al. (Human Genet 1992, Vol. 90: 299-302), Tuschl et al. (US 2004/0259247), Fosnaugh et al. (US 2003/0143732), and Holen et al. (Nucleic Acids Research, 2002, Vol. 30, No. 8).

The instant claims are drawn to a double stranded oligoribonucleotide wherein one strand comprises consecutive sequences from SEQ ID Nos. 3 and 25, and further drawn to a vector and a composition comprising said oligoribonucleotide.

Rao et al. teach the gene for bone morphogenetic protein 2A (BMP2a) and teach BMP2A is thought to be involved in cartilage and bone formation during embryogenesis in mice and is thought to be the gene in humans for the autosomal dominant disease fibrodysplasia (see page 299). Roa et al. teach said gene has been mapped to chromosome 20 and speculates that the gain or loss of function of said gene might be involved in specific malformations (see page 301).

At the time of filing of the instant invention, it was well known in the art that RNAi using siRNA was becoming a more efficient method of silencing gene expression. Tuschl et al. teach making and using siRNA for mediating gene silencing (see Example 1 and the siRNA User Guide beginning at paragraph 0178) and has demonstrated

siRNA mediated silencing in mammalian cells and states that the use of short siRNAs holds great promise for inactivation of gene function in human tissues to study the role genes play in progression of certain diseases and the development of gene-specific therapeutics (see paragraphs 0144-0151).

Fosnaugh et al. describes making siRNA reagents useful for modulating gene expression. Fosnaugh et al. teach identification of siRNA targets sites in any RNA sequence by screening the mRNA transcript using a computer folding algorithm and describes siRNA that target a gene from a database, such as Genbank (see Example 2). Fosnaugh et al. teach using target sites that are known or have been determined as effective based on studies with other nucleic acid molecules such as antisense can be used to design siRNA as well as target sites known to be associated with disease or conditions such as those containing mutations or deletions (see Example 2). In Example 3, Fosnaugh et al. details selection of siRNA target sites in RNA and screening of siRNA to access activity. Fosnaugh et al. teach the siRNA molecules are comprised of two strands which are 18 to 24 nucleotides in length (see paragraph 0122) or can be a hairpin structure (see paragraph 0057) and optionally further comprises nucleotide overhangs on either the 5' or 3' terminal ends (see paragraph 0058). Fosnaugh et al. teach the siRNA can be expressed from expression vectors comprising various promoters such as pol III promoters and termination signals (see paragraph 0220-0223).

Holen et al. teach design and testing of siRNA molecules ability to mediate RNAi and demonstrate the routine nature of finding a siRNA with optimal activity when the

target region is known. Holen et al. teach designing multiple siRNA along the entire length of a target gene wherein the siRNA sequence was shifted by three nucleotides and found varying degrees of activity and concluded the efficiency of siRNAs is depended on the target positions (see entire reference, particularly pages 1458-1459).

It would have been obvious to one of skill in the art at the time the invention was made to use the methods taught by Fosnaugh et al. to make a dsRNA and a composition capable of targeting a gene encoding BMP2A.

One of ordinary skill in the art would have been expected to be able to design any siRNA targeted to any viral transcript because Fosnaugh et al. details the steps to effectively find a target site in any RNA and design and test siRNA molecules for specific RNAi activity. Fosnaugh et al. teach known target sites that have previous been targeted by other inhibitory compounds are useful as well as known target sites that have been shown in art to be responsible for certain disease. It was well known in the art at the time of the invention that siRNA molecules could be designed and tested for optimal activity as shown by Holen et al.

One of ordinary skill in the art would have been expected to be able to design any siRNA targeted to any mRNA transcript because Fosnaugh et al. details the steps to effectively find a target site in any RNA and design and test siRNA molecules for specific RNAi activity. Fosnaugh et al. teach known target sites that have previous been targeted by antisense compounds are useful as well as known target sites that have been shown in art to be responsible for certain disease. Tuschl et al. teach that it was well recognized in the art that siRNA was a more efficient method of silencing gene

expression, requiring concentrations far less than the methods of the prior art, such as antisense compounds. In looking to reduce gene expression of BMP2A mRNA to study the role and function of said gene, one of ordinary skill in the art would have wanted use the most efficient method to silencing gene expression and would have looked to the teachings of Tuschl et al. and Fosnaugh et al. for generation of siRNAs targeted to BMP2A mRNA. Tuschl et al. and Fosnaugh et al. teach that production of siRNAs to any target gene is a matter of routine experimentation and optimization and clearly set forth the guidelines to design such molecules. Thus it would have been a matter of routine experimentation to make a siRNA molecule targeted to BMP2A comprising SEQ ID No. 3.

Finally, one of ordinary skill in the art would have expected to be able to generate a siRNA targeted to a BMP2A mRNA gene given Tuschl et al. and Fosnaugh et al. teach the basic steps to identifying any target site and making and screening siRNA molecules for activity, steps that are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Primary Examiner
Art Unit 1635